

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

- 1 1. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein
2 comprising
3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;
5 and
6 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
7 binds to a protein overexpressed on the surface of a cell.
- 1 2. (Original) The nucleic acid of claim 1, wherein the matrix
2 metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9
3 (gelatinase B) and membrane-type1 MMP (MT1-MMP).
- 1 3. (Original) The nucleic acid of claim 1, wherein the plasminogen activator
2 is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase
3 plasminogen activator (u-PA).
- 1 4. (Previously Presented) The nucleic acid of claim 1, wherein the matrix
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID
3 NO: 20).
- 1 5. (Previously Presented) The nucleic acid of claim 1, wherein the
2 plasminogen activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID
3 NO: 23), GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1 6. (Original) The nucleic acid of claim 1, wherein the protein overexpressed
2 on the surface of a cell is a receptor.

1 7. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide comprises a cytokine.

1 8. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide comprises a growth factor.

1 9. (Original) The nucleic acid of claim 1, wherein the heterologous
2 polypeptide is a member selected from the group consisting of: IL-2, GM-CSF, and EGF.

1 10. (Original) The nucleic acid of claim 1, comprising the nucleotide
2 sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1 11. (Original) A vector comprising the nucleic acid of claim 1.

1 12. (Original) The nucleic acid of claim 6, wherein the cell is a cancer cell.

1 13. (Original) The nucleic acid of claim 7, wherein the heterologous
2 polypeptide comprises GM-CSF.

1 14. (Original) The nucleic acid of claim 7, wherein the heterologous
2 polypeptide comprises IL-2.

1 15. (Original) The nucleic acid of claim 8, wherein the heterologous
2 polypeptide comprises EGF.

1 16. (Original) A nucleic acid encoding a Diphtheria toxin fusion protein
2 comprising

3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and

5 (2) GM-CSF.

1 17. (Original) A polypeptide encoded by the nucleic acid of claim 1.

1 18. (Original) A polypeptide encoded by the nucleic acid of claim 10.

1 19. (Original) A polypeptide encoded by the nucleic acid of claim 16.

1 20. (Original) A host cell comprising the vector of claim 11.

1 21. (Original) The nucleic acid of claim 12, wherein the cancer is leukemia.

1 22. (Original) The nucleic acid of claim 12, wherein the cancer is acute
2 myelogenous leukemia.

1 23. (Original) A pharmaceutical composition comprising the protein of claim
2 18 and a pharmaceutically acceptable carrier.

1 24. (Currently Amended) A method of treating cancer, the method
2 comprising administering to a subject a Diphtheria toxin fusion protein comprising
3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator;
5 and

6 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
7 binds to a protein overexpressed on the surface of a **cancer** cell.

1 25. (Original) The method of claim 24, wherein the matrix metalloproteinase
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and
3 membrane-type1 MMP (MT1-MMP).

1 26. (Original) The method of claim 24, wherein the plasminogen activator is
2 selected from the group consisting of t-PA and u-PA.

1 27. (Previously Presented) The method of claim 24, wherein the matrix
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ (SEQ ID
3 NO: 20).

1 28. (Previously Presented) The method of claim 24, wherein the plasminogen
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1 29. (Original) The method of claim 24, wherein the protein overexpressed on
2 the surface of a cell is a receptor.

1 30. (Original) The method of claim 24, wherein the cell is a cancer cell.

1 31. (Original) The method of claim 24, wherein the heterologous polypeptide
2 comprises a cytokine.

1 32. (Original) The method of claim 24, wherein the heterologous polypeptide
2 comprises a growth factor.

1 33. (Original) The method of claim 24, wherein the fusion protein is encoded
2 by the nucleotide sequence set forth in SEQ ID NO: 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13.

1 34. (Original) The method of claim 30, wherein the cancer is leukemia.

1 35. (Original) The method of claim 30, wherein the cancer is acute
2 myelogenous leukemia.

1 36. (Original) The method of claim 31, wherein the heterologous polypeptide
2 comprises GM-CSF.

1 37. (Original) The method of claim 31, wherein the heterologous polypeptide
2 comprises IL-2.

1 38. (Original) The method of claim 32, wherein the heterologous polypeptide
2 comprises EGF.

1 39. (Original) The method of claim 24, wherein the Diphtheria toxin fusion
2 protein comprises:

3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and

5 (2) GM-CSF.

1 40. (Currently Amended) A method of targeting a compound to a cancer cell
2 overexpressing a cytokine receptor or a growth factor receptor, the method comprising the steps
3 of:

4 administering to the cell Diphtheria toxin fusion protein comprising

5 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
6 been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and
7 wherein the Diphtheria toxin is cleaved by a matrix metalloproteinase or a plasminogen
8 activator; and

9 (2) a heterologous polypeptide, wherein the heterologous polypeptide specifically
10 binds to a cytokine receptor or a growth factor receptor.

1 41. (Currently Amended) The method of claim 40, wherein the cell **also**
2 overexpresses a matrix metalloproteinase, a tissue plasminogen activator, or a urokinase
3 plasminogen activator.

1 42. (Original) The method of claim 40, wherein the matrix metalloproteinase
2 is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and
3 membrane-type1 MMP (MT1-MMP).

1 43. (Original) The method of claim 40, wherein the plasminogen activator is
2 selected from the group consisting of t-PA and u-PA.

1 44. (Previously Presented) The method of claim 40, wherein the matrix
2 metalloproteinase cleavage sites are GPLGMLSQ (SEQ ID NO: 19) and GPLGLWAQ SEQ ID
3 NO: 20).

1 45. (Previously Presented) The method of claim 40, wherein the plasminogen
2 activator cleavage site is selected from the group consisting of QRGRSA (SEQ ID NO: 23),
3 GSGRSA (SEQ ID NO: 21) and GSGKSA (SEQ ID NO: 22).

1 46. (Original) The method of claim 40, wherein the cancer cell is a leukemia
2 cell.

1 47. (Original) The method of claim 40, wherein the cancer cell is an acute
2 myelogenous leukemia cell.

1 48. (Original) The method of claim 40, wherein the Diphtheria toxin fusion
2 protein comprises

3 (1) residues 1-388 of Diphtheria toxin, wherein the native furin cleavage site has
4 been substituted for a cleavage site for a urokinase plasminogen activator; and

5 (2) GM-CSF.

1 49. (Currently Amended) An isolated nucleic acid comprising the sequence
2 set forth in any one of ~~SEQ ID NOS: 2-18~~ **SEQ ID NOS: 2-13 or SEQ ID NOS: 15-18.**